EXPRESS MAIL NO. EV348173476US

Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Stephen C. Goshorn, et al.
Application No.:	09/589,870
Filed:	June 5, 2000
For:	*STREPTAVIDIN EXPRESSED GENE FUSIONS AND METHODS OF USE THEREOF*

Examiner	:	Stephen L. Rawlings, Ph.D.
Art Unit	:	1642
Docket No.	:	690022.547

DECLARATION OF STEPHEN C. GOSHORN, PH.D. UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Stephen C. Goshorn, a citizen of the United States, declare and state that:

1. I am a scientist, previously employed at NeoRx Corporation, Seattle, Washington, United States, and co-inventor on the above-identified patent application (hereinafter referred to as "instant application").

2. I have reviewed the Office Action dated January 13, 2003 and the Examiner's rejection of claims 18-39 and 65 of the instant application under 35 U.S.C § 103(a). I am providing this Declaration for the purpose of assisting the Examiner in evaluating the evidence of secondary considerations, in particular, heretofore unrecognized advantages over the prior art with regard to the instant invention.

3. Described below is evidence clearly showing that the instant invention comprising genomic streptavidin fusion proteins displays unexpected advantages as compared to core streptavidin of the prior art.

(a) Nowhere is the use of genomic streptavidin in fusion proteins described or suggested in the cited prior art. The references cited in the Office Action, in particular Dubel *et al.* and Pahler *et al.*, describe only the use of core streptavidin. In fact, Pahler *et al.* actually teaches away from using the parent molecule (genomic streptavidin) in fusion proteins by stating that core streptavidin is more soluble than the parent molecule (see Abstract). This statement by Pahler *et al.* further underscores the unexpected finding of the instant invention that genomic streptavidin expressed gene fusions are expressed as soluble proteins.

Prior to the instant invention, preparations of streptavidin expressed gene fusions have been made by expressing a core streptavidin-containing construct in bacteria, wherein inclusion bodies are formed. Such production has several disadvantages, including the rigor and expense of purifying from inclusion bodies, the necessity of using harsh denaturing agents such as guanidine hydrochloride, and the difficulty in scaling up in an economical fashion.

(b) The instant invention provides the following unexpected advantages:

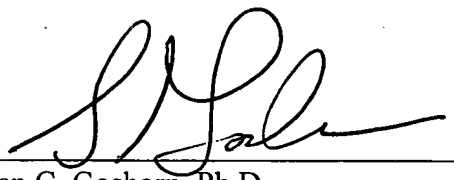
1. Genomic streptavidin expressed gene fusions are expressed as a soluble protein into the periplasmic space of bacteria where said protein undergoes spontaneous folding.

2. The periplasm is a low biotin environment and, therefore, it is not necessary to purify and refold the protein under harsh denaturing conditions that may prove fatal to the polypeptide encoded by a heterologous nucleic acid molecule fused to the genomic streptavidin nucleic acid molecule.

3. The above unexpected properties of using genomic streptavidin in the production of fusion proteins allow for an easy, cost effective, and scalable method for the production of streptavidin fusion proteins.

Thus, the instant invention provides unexpected advantages not described or suggested in the prior art.

4. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements, and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.



Stephen C. Goshorn, Ph.D.

6-22-03

Date

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